APPLICANT(S): CANAANI, Dan et al.

SERIAL NO.:

09/975,300

Page ?

October 12, 2001

Page 2

In the claims:

- 1. (Amended) A method for screening a molecule, wherein said molecule is a chemical compound, or a drug which have has a synthetic lethal property, when in combination with a gene of interest carrying a non-lethal mutation, said method comprising the steps of:
- i. transfecting a first reporter gene, as part of an integration plasmid, into mammalian cells having a genome comprising a gene of interest which carries a nonlethal mutation, or a genome which is null of said gene of interest;
 - ii. selecting clones stably expressing said first reporter gene;
- iii. introducing into said cells a survival plasmid comprising a functioning copy of said gene of interest, a second reporter gene, selectable marker, an origin of DNA replication and a nuclear antigen gene essential for replication of the plasmid within said cells, wherein said survival plasmid is autonomously replicating and spontaneously lost from said cells;
 - vi. growing said cells in the presence of a selection compound which selects for said selectable marker;
 - vii. selecting cell clones stably expressing said second reporter gene and said functioning copy of said gene of interest;
 - viii. removing <u>said</u> selection <u>compound</u>, <u>for the which selects for said</u> selectable marker, and adding molecules destined for screening of their ability to impose selective pressure enforcing retention of the unstable survival plasmid.
 - ix. determining survival plasmid retention in cells <u>by measuring the</u> <u>expression ratio of second's to first reporter gene</u>, <u>wherein</u>, if the survival plasmid <u>retains</u>, the molecule has <u>thus identifying a molecule having</u> a synthetic lethal property when in combination with <u>a</u> non lethal mutated gene of interest.
 - 2. (Original) The method according to Claim 1, wherein said selectable marker is a dominant selectable marker.

APPLICANT(S): CANAANI, Dan et al.

SERIAL NO.: 09/975,300

FILED:

October 12, 2001

Page 3

3. (Original) The method according to Claim 1, wherein said cells are human cells.

- 4. (Original) The method according to Claim 1, wherein said cells are rodent cells.
- 5. (Amended) The method according to Claim 1, wherein the products of said first <u>reporter gene</u> and second reporter gene are fluorescent proteins.
- 6. (Original) The method according to Claim 5, wherein the product of said first reporter gene has an excitation and/or emission peak which differs from the excitation and/or emission peak of the product of said second reporter gene.
- 7. (Amended) The method according to Claim ‡ 3, wherein said human cells are human cancer cells.
- 8. (Original) The method according to Claim 7, wherein said gene of interest is specifically incapacitated in human cancer cells.